

Evaluation of a computer-based cognitive training program for early-stage Alzheimer's disease

Cognitive training in AD

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Abstract

Aim: Previous studies have reported that computer-based cognitive training (CBCT) programs improve many cognitive functions, especially memory, attention, and executive functions in early-stage Alzheimer's disease (AD) patients. In addition, these programs have been shown to improve patients' mood and quality of life. In this study, it was aimed to investigate the effect of a CBCT program on cognitive functions, behavioral symptoms, and quality of life in early-stage AD patients.

Material and Methods: Twenty-nine patients with a diagnosis of probable AD were included in the study. Patients and their caregivers were examined neuropsychologically before and after (after 12 weeks) the CBCT program. Mini-Mental State Examination (MMSE), forward and backward digit span, clock drawing test (CDT), verbal fluency tests, and Trail Making Test A and B forms were used for cognitive assessment, and the Geriatric Depression Scale (GDS) was used for depression screening. In addition, patients and their caregivers were evaluated with the Quality of Life in Alzheimer's Disease Scale, the Caregiver Burden Scale, the Caregiver Stress Scale, and the Reactions to Helping Your Family Member Scale.

Results: Forward and backward digit span tests at the end of the program were significantly better than those before the program (4.81 ± 0.75 , $p=0.01$ / 10.72 ± 5.64 , $p=0.01$, respectively). In addition, it was observed that the trail-making test form B was completed faster at the end of the program (308 ± 166.66 s, 200 ± 111.73 s; $p=0.02$). The reaction times of the patients at the end of the program were significantly shorter than those before ($p=0.01$).

Discussion: The results indicate that the 12-week CBCT program provides an improvement in simple and sustained attention, delayed recall, executive functions, and information processing speed in early-stage Alzheimer patients. Large-scale randomized controlled studies are needed to more clearly demonstrate the effects of such programs on cognitive and behavioral symptoms, quality of life, and caregiver burden of AD.

Keywords

Computer-Based Cognitive Training, Cognitive Functions, Quality of Life, Caregiver Burden

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Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disease that affects all cognitive domains, especially memory, and activities of daily living (ADLs) [1]. Difficulties in cognitive functions vary depending on the stage of the disease. In early-stage AD, which is considered the first stage, symptoms such as mild forgetfulness noticed by family members or friends, inability to learn new things, difficulty in finding words, losing belongings, and withdrawal from social life are seen. Despite difficulties in more than one cognitive domain, patients' functionality is relatively good and they can live independently [2]. Even in early-stage AD, the quality of life of patients and caregivers is adversely affected [3].

Since the effects of acetylcholinesterase inhibitors and memantine used in treatment are limited, nonpharmacological methods have recently been focused on in addition to pharmacological treatment. It is thought that cognitive-based therapies may be effective in reducing cognitive deficit in AD [4]. Among these interventions is cognitive training, which involves performing a standard group task that reflects cognitive functions such as memory, attention, and problem-solving [1]. It is known that computer-based cognitive training (CBCT) programs, especially those personalized and gradually increasing in difficulty according to patient performance, are the most beneficial method in early-stage AD [5]. Similarly, these programs have been reported to improve many cognitive skills, including memory performance, compared to the traditional paper-and-pencil method [6].

Although the effectiveness of the exercises in these programs on which cognitive functions in early-stage AD is unclear, studies show that they can result in improvement in memory, executive functions, naming, attention, semantic fluency, and speed of information processing skills [7]. It is also known that they improve the quality of life of patients and their caregivers and do not increase caregiver burnout [8].

The aim of the present study was to investigate the effects of a CBCT program on cognitive functions and behavioral symptoms in early-stage Alzheimer's patients. In addition, this program is intended to evaluate the quality of life of patients and caregivers and the burden on caregivers.

Material and Methods

Patients

Fifty-one possible AD patients who presented to the neurology outpatient clinic were evaluated. All patients were in the mild stage of dementia (Clinical Dementia Rating: 1). Patients who had severe hearing and vision problems that would prevent them from complying with the CBCT program, those with severe systemic or psychiatric diseases, and those who did not volunteer to participate in the program were excluded from the study. Twenty-nine early-stage Alzheimer's patients who met the appropriate criteria were included in the study (Figure 1). Age, sex, educational status, marital status, systemic diseases, family history of dementia, disease duration (according to symptom onset), and anti-dementia drugs (donepezil, rivastigmine, memantine) used were recorded.

Ethics committee approval was obtained for the study (Scientific Research Ethics Committee of Gulhane Training and Research

Hospital, Project/Decision No: 2020-511, Date: 29.12.2020) and necessary consents were obtained from the relatives of the patients that their data could be used for scientific purposes.

Neuropsychological evaluation

Neuropsychological tests were performed by a neuropsychologist specialized in this field before and at the end of the CBCT program (12 weeks after the initial evaluation). The patients' global cognitive performance was evaluated using the Turkish version of the Mini-Mental State Examination (MMSE) [9]. Additional detailed neuropsychological tests were administered to assess the following areas: (1) visuospatial functions, sequencing, planning, and abstract thinking (clock drawing test) [10]; (2) attention (forward and backward digit span tests) [11]; (3) ability to produce words, short- and long-term memory, perseveration, and sustained attention (verbal fluency tests) [12]; (4) visual-motor tracking, psychomotor speed, mental flexibility, visual attention, and executive functions (trail making test forms A and B) [13].

The Turkish version of the Geriatric Depression Scale was used to evaluate the emotional state of the patients [14]. Their performance in terms of activities of daily living (ADLs) was established using the Barthel ADL Index [15].

In addition, patients and their caregivers were examined in terms of their quality of life, caregiver stress and burden [16-19].

The four-point (0-4 points) scoring system was used because it was relatively easier for the clock drawing test (CDT). In the four-point system, one point each is given for a closed circle, digits in the correct positions, all 12 digits, and the correct position of the clock hands to show 11:10. The highest score that can be obtained from this version of the CDT is 4 and the lowest score is 0.

In the digit span tests applied to evaluate simple attention, random 2- to 8-digit sequences were given for the forward span and 2- to 7-digit sequences for the backward span. One point was given for each item counted correctly.

In the verbal fluency tests, letter fluency (producing words starting with the letters K, A, and S in one minute) and semantic fluency (producing words from the animal category in one minute) were evaluated. The numbers of words produced were recorded.

In the trail making tests, completion times, totals, differences, and ratios of the times and the number of errors obtained from both forms (A and B) were calculated.

In the Barthel ADL Index, which examines ten activities of daily living, a score of 0-20 indicates full dependence, 21-61 points indicate severe dependence, 62-90 points indicate moderate dependence, 91-99 points indicate mild dependence, and 100 points indicate full independence.

The geriatric depression scale consists of 30 questions and evaluates mood over the last week. Scores of 0-10 indicate no depression, 11-13 probable depression, and 14 and above definite depression.

The Quality of Life in AD Scale and its family version assess five sub-dimensions (social interaction, self-awareness, affect and mood, enjoyment of activities, and interaction with the environment). A low score on the scale indicates the impaired quality of life.

The caregiver burden scale, on the other hand, is used to evaluate the stress experienced by caregivers. With this scale, caregivers' relationships with their patients, general health status, emotional difficulties, social life, and economic difficulties during the care process are evaluated. It consists of 22 items that determine the effect of caregiving on a person's life and each is scored between 0 and 4. A score of 0-20 points indicates little/no load, 21-40 moderate load, 41-60 severe load, and 61-88 overload.

The Caregiver Stress Scale is a 13-item scale involving job status, financial status, physical condition, social status, and time. Each question is scored as 0 or 1, with a higher score indicating a higher level of stress.

The Reactions to Helping Your Family Member Scale is a 15-item scale included in the Family Caregiving Inventory. The participants are requested to respond to the items in the scale as follows: 0 - Not at all, 1 - Very little, 2 - A little, 3 - Quite a lot, 4 - A lot. High scores obtained from the scale indicate that caregivers react more to their relatives during care.

NoroSOFT® Cognitive Training Program

The NoroSOFT® Cognitive Training Program includes exercises culturally appropriate for Turkey in Turkish that can be applied via the Internet that improve memory, attention and concentration, executive functions, visual-spatial perception, and conceptualization skills. As the total daily score (determined from the answers and reaction times) increases, the exercises become more difficult. In each session, lasting approximately 25-30 minutes, a total of ten exercises, two from each of these five cognitive domains, were applied to the participants (3 days a week for 12 weeks). The patients were permitted to continue taking their current medication.

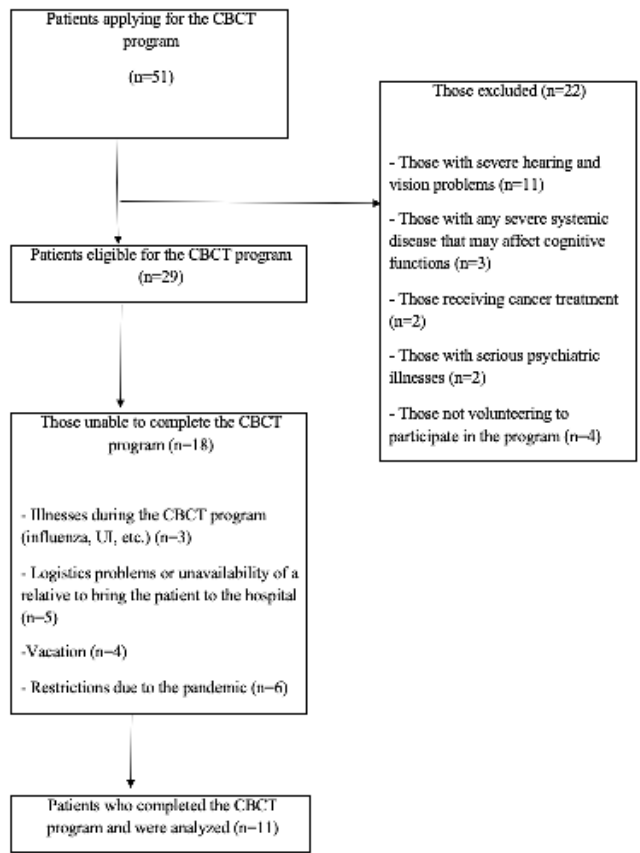


Figure 1. Early-stage Alzheimer’s patients included in the study

In addition, the reaction times of all patients in the first and last sessions they performed in the CBCT program were recorded in seconds.

Statistical analysis

SPSS 21.0 (Statistical Package for the Social Sciences, Chicago, IL, USA) was used for statistical analysis. Descriptive statistics were expressed as mean ± standard deviation for continuous and discrete numerical variables and as number of patients and percentages for nominal variables. The data expressed as percentages were compared using the Fisher–Freeman–Halton test and the chi-square test, and continuous variables were compared using the Mann–Whitney U test. The p- values < 0.05 were considered statistically significant.

Results

In the present study, 51 patients diagnosed with early-stage AD were evaluated. Twenty-two of the patients were not included in the CBCT program for various reasons. The remaining 29 patients were eligible for the program. However, 18 patients were unable to complete the program due to infection; logistical problems or relatives not being available to bring the patient to the hospital; the patient and/or their relatives going on vacation during the program, or the lockdown for people over 65 years old during the pandemic. The data of 11 patients [9 males (81.8%), 2 females (18.2%)] who completed the program were analyzed. The mean age of the female patients was 66.50 ± 4.94 years and of the male patients was 72.77 ± 7.87 years. All patients were married. Only 2 patients (18.2%) had no systemic disease. Approximately half of them had a family history of dementia (n=5, 45.5%). The mean duration of education of the patients was 7.63 ± 2.76 years and the mean duration of the

Table 1. Neuropsychological assessment scores before and after the CBCT program

	Scores before the program	Scores after the program	p
MMSE (mean ±SD)	24.27±3.31	25.72±2.49	0.06
Orientation	8.72±1.67	8.90±1.57	0.64
Registration	2.90±0.30	3.0±0.0	0.34
Attention	3.63±1.85	4.54±0.68	0.17
Recall	0.36±0.67	0.45±0.52	0.72
Language	8.63±0.67	8.81±0.40	0.34
CDT (mean ±SD)	3.54±0.68	3.72±0.46	0.44
Phonemic fluency (mean ±SD)	6.72±2.41	7.90±3.56	0.24
Semantic fluency (mean ±SD)	13.36±4.05	13.45±4.65	0.90
Forward digit span (mean ±SD)	4.81±0.75	10.72±5.64	0.01*
Backward digit span (mean ±SD)	2.81±1.53	6.18±3.76	0.01*
Trail Making Test A (n=11) (mean ±SD)			
Duration (s)	82.72±38.18	72.72±53.83	0.16
Errors	0.2±0.42	0.3±0.48	0.67
Trail Making Test B (n=9) (mean ±SD)			
Duration (s)	308±166.66	200±111.73	0.02*
Errors	3.4±2.83	2±2.12	0.28
B-A (n=9)(s) (mean ±SD)	236.55±157.03	146.88±106.07	0.04*
A+B (n=9)(s) (mean ±SD)	380.55±177.27	254.22±119.39	0.01*
B/A (n=9) (mean ±SD)	4.36±2.11	3.78±2.0	0.27

SD: Standard deviation, MMSE: Mini-Mental State Examination, CDT: Clock drawing test s: second, *p value < 0.05

Table 2. Additional neuropsychological assessment scores before and after the CBCT program

	Scores before the program	Scores after the program	p
ADLs (mean ±SD)	98.18±2.52	98.18±2.52	1
GDS (mean ±SD)	7.54±3.61	6.27±3.82	0.17
QOL-AD Scale (mean ±SD)	35.81±6.33	36.90±7.34	0.38
Family version (mean ±SD)	33.72±5.06	33.18±6.11	0.76
Caregiver Burden Scale (mean ±SD)	23.81±10.58	28.09±13.70	0.28
Caregiver Stress Index (mean ±SD)	2.72±2.37	3.81±3.97	0.30
Reactions to the family member (mean ±SD)	15.09±8.23	20.63±14.65	0.09

SD: Standard deviation, ADLs: Activities of daily living index, GDS: Geriatric Depression Scale, QOL-AD Scale: Quality of Life in Alzheimer's Disease Scale, *p value < 0.05

disease was 1.63 ± 0.80 years. All patients were treated with donepezil 10 mg/day.

The neuropsychological test scores of the patients and their caregivers before and after the CBCT program (approximately 12 weeks after the end of the program) are summarized in Table 1 and Table 2. It is seen that the forward and backward digit span tests at the end of the program were significantly better than before the program (4.81 ± 0.75, p=0.01 / 10.72 ± 5.64, p=0.01, respectively). In addition, the Trail Making Test form B was completed faster at the end of the program (308 ± 166.66 s, 200 ± 111.73 s, p=0.02). As expected, due to this decrease in duration for the B form, the difference and total scores of the two forms of the Trail Making Test improved significantly at the end of the CBCT program (p=0.04 and p=0.01). The MMSE, CDT, verbal fluency, ADL, and GDS scores of the patients before and after the program were similar. No significant difference was seen in the quality of life of the Alzheimer's patients or their family members, caregiver burden or stress, or reactions to family members.

The mean reaction time in the first session, when the patients started the CBCT program, was 82.05 ± 46.98 s. The mean reaction time in the last session of the 12-week program was 48.90 ± 16.35 s. Reaction times at the end of the program were significantly better than those before (p=0.01).

Discussion

The results of this study showed that a 12-week CBCT program improved simple and sustained attention, delayed recall, executive functions, and information processing speed in early-stage Alzheimer's patients. However, the program did not affect the quality of life of patients and their caregivers, depressive mood, or caregiving burden.

Recently, it has been stated that cognitive training practices can be effective in reducing the progression of AD in addition to medical treatment. [4]. It is known that CBCT programs in particular are more effective than the traditional paper-and-pencil method [5,6]. Cinar and Sahiner reported that after at least a 1200-minute CBCT program, the scores of early-stage AD patients receiving rivastigmine treatment from the Montreal Cognitive Assessment (MoCA) Scale, which was developed for the screening of mild cognitive impairment, increased significantly, whereas MoCA scores of the patients in the control group decreased [20]. Similarly, a meta-analysis of 12 studies revealed that such computer-based programs had a moderately

positive effect on cognition [5]. In a small review of randomized controlled CBCT study results, these interventions were found to be ineffective in terms of basic cognitive functions. However, it has been suggested that these exercises may provide some positive effects in improving behavioral symptoms as well as the learning and short-term memory performance of patients with mild cognitive impairment and/or dementia [21]. In our study, it was seen that the cognitive functions of the patients improved after the CBCT program, which was consistent with previous studies.

Although it is not clear which cognitive functions these exercises improve, it has been observed that they improve attention, delayed recall and working memory, semantic fluency, naming, visuospatial skills, and executive functions [7,22]. The results of our study similarly revealed improvements in attention, delayed recall, and executive functions in patients. Unlike previous studies, there was no difference in semantic fluency or visuospatial skills. This may have been due to the number of patients analyzed.

In addition, the patients in the present study exhibited a significant increase in information processing speed at the end of the program. This result is consistent with previous studies stating that CBCT programs increase information processing speed [7].

The CBCT program can improve the behavioral symptoms of early-stage AD patients and the quality of life of both patients and their relatives. With these treatments, depression and apathy in patients can be reduced [5,23]. A reduction in the neuropsychiatric symptoms of patients also has a positive effect on caregiver burnout and stress [24]. It has been reported that these programs do not increase caregiver emotional burnout compared to controls, and they even reduce caregiver burnout associated with daily activities one year later [8]. Cognitive training is an approach that also improves the quality of life of patients and their caregivers [25]. In our study, the patients' depressive moods and quality of life and the caregivers' stress levels, caregiver burden, and quality of life after the CBCT program were similar to those before the program. The fact that there was no change in these areas in the patients or their caregivers over the 12 weeks and there was no worsening suggests that the CBCT program is beneficial, even if there is no statistically significant difference.

The effects of these programs on the ADLs of early-stage AD patients varied between different studies. While it was reported that cognitive training increased independent activities, it had no effect on ADL in some studies [5,8,20]. Our results also indicated that there was no positive effect on ADLs.

Cognitive training creates changes in the structure and function of synapses, improving neuronal connections and increasing neurogenesis. Thus, it is thought that these exercises can improve cognition by altering brain functions at both the synaptic and molecular levels [1,3].

The present study had some limitations. Although patients were evaluated in detail before and after the CBCT program using standardized neuropsychological tests, the lack of a control group is the most important limitation. At the same time, the number of patients analyzed in our study is relatively small.

Conclusion

In addition to pharmacological treatment in early-stage Alzheimer's patients, it is important to implement easily applicable and accessible CBCT programs without side effects. Large-scale randomized controlled studies are needed to more clearly demonstrate the effects of such programs on cognitive and behavioral symptoms, quality of life, and caregiver burden in early-stage AD.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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